REMARKS

I. Status of the Application

Claims 1-18 are presently pending in the application. Claims 1-18 stand rejected under 35 USC §112, first paragraph as lacking adequate written description. Claims 14-18 stand rejected under 35 USC §112, second paragraph as being indefinite. Claims 1, 4, 6-8 and 13 stand rejected under 35 USC §102(b) as being anticipated by Lynch US 6,207,397. Claims 1-4, 6-11 and 13-18 stand rejected under 35 USC §103(a) as being unpatentably obvious over Keating (June 2000) in view of Zuccola (Feb. 2000). Claims 1, 4-8, 12 and 13 stand rejected under 35 USC §103(a) as being unpatentably obvious over Lynch in view of Gee US 6,162,931.

Applicants have amended the claims to more clearly define and distinctly characterize Applicants' novel invention. Specifically, claim 1 has been amended to recite first and second viral polymerase subunits or fragments thereof which are capable of interacting together. Support for the amendment can be found at page 8 lines 25-29 where Applicants teach that "[f]or example, in the case of many viral polymerases, a fragment of a catalytic subunit (or the entire catalytic subunit as the case may be) can interact with a fragment of processivity subunit (or the entire processivity subunit as the case may be) to form a functional protein, e.g. a functional polymerase capable of synthesizing viral DNA." Accordingly, the amendments add no new matter.

Applicants request entry and consideration of the foregoing amendments and reconsideration of the application in view of the following remarks, which are intended to place this case in condition for allowance.

II. The Specification Provides Adequate Written Description for the Claims

On page 2 of the instant Office Action, claims 1-18 stand rejected under 35 USC 112, first paragraph as lacking adequate written description insofar as the Examiner believes the claims include "a huge number of mutually associating proteins, completely unrelated to HSV polymerase." Applicants respectfully traverse the Examiner's rejection as to the amended claims now presented which are directed to viral polymerase subunits or fragments thereof that are capable of interacting together.

Applicants claimed subject matter (as it relates to claim 1) is directed to a method for identifying inhibitors of interaction between viral polymerase subunits where test compounds are screened for their ability to inhibit subunit interaction between a first viral polymerase subunit or fragment thereof and a second viral polymerase subunit or fragment thereof that are capable of subunit interaction. Claim 14 is specific to herpes simplex virus. The inhibition of the interaction of the two viral polymerase subunits or fragments thereof is determined by fluorescence polarization. Should the assay identify a test compound that inhibits subunit interaction, a further assay could be conducted to determine whether the test compound has antiviral activity.

To satisfy the written description requirement, the specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention (MPEP 2163(I)). There is no requirement for a verbatim description of every claimed embodiment. When deciding whether a disclosure satisfies the written description requirement with regard to a specific claim, one should examine the application as a whole to decipher what it conveys to one skilled in the pertinent art. The descriptive text needed to meet the written description requirement varies with the nature and

scope of the invention at issue, and with the scientific and technologic knowledge already in existence.

Applicants note that the Examiner has not objected to the claimed method steps per se, namely to assay test compounds which inhibit subunit interaction using fluorescence polarization. Instead, the sole basis for rejecting the claims as lacking adequate written description is the Examiner's belief that the scope of compounds covers a "huge number."

However, there is a strong presumption that claims as originally filed meet the written description requirement of 35 U.S.C. § 112, first paragraph. Further, the claims are plainly worded such that one skilled in the art would readily understand that the nature of the invention is to begin with viral polymerase subunits or fragments thereof ***that are capable of interacting*** and then to screen compounds to identify those that inhibit the interaction. The goal, of course, is to identify compounds having antiviral activity.

Applicants respectfully submit that the as-filed specification provides sufficient written description such that one of skill in the art would readily understand the nature and scope of the method invention using the claimed viral polymerase subunits or fragments thereof. The invention is not the discovery of viral polymerase structure or function, but rather their use in the claimed screening method. Where the prior art identifies exemplary viral polymerase subunits, the as-filed specification is not per se required to disclose an exhaustive list of such information verbatim. One skilled in the art would know of the existence of such viral polymerase subunits.

In addition, the claims clearly describe the requirement for functionality of the claimed viral polymerase subunits or fragments thereof insofar as they are required interact. Such interaction is widely understood by those of skill in the art. The scope of the claims is not so broad as to include any two proteins that happen to bind together. The specification provides

written description that fragments can be used. A requirement that these viral subunits be analyzed and reported *ipsis verbis* in the specification does not add descriptive substance. Nevertheless, Applicants disclose subunits and their public availability at page 12. Additional references describing HSV DNA polymerase and fragments are provided at pages 16-17 and in Example 1.

Applicants further describe the synthesis and expression of fragments, specific examples of conducting the polarization assays, and describe the testing compounds that elicit a decrease in polarization assays through different exemplary processes. While many of the processes were conducted on exemplary fragments, one skilled of the art will readily understand how to conduct the various methods of the disclosure with other fragments. This is especially true in view of the voluminous articles and patents incorporated by reference that readily convey the functional and chemical properties of the fragments, background information and methods. (*See, e.g.*, Specification; pages 21 and 31 – 33).

Applicants' specification when combined with the knowledge of one of skill in the art meets the written description requirement by demonstrating that Applicants had possession of the claimed invention. One of skill in the art would not be prohibited, and in fact would be encouraged, to look to readily available literature references for published viral polymerases having subunits that interact. The specification and claims impose these functional requirements on the claimed fragments as well. Once identified, the specification teaches how one of skill in the art can use the viral polymerase subunits or fragments thereof in the method of screening inhibitor compounds using fluorescence polarization. Accordingly, one of skill in the art, based on the specification and her own knowledge, could precisely envision or readily determine with

resort to publicly available information, the claimed viral polymerase subunits or fragments thereof which interact together.

III. Claims 14-18 Are Definite

Claims 1-18 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse the rejection in view of the Remarks below.

The Examiner first asserts that the term "substantially homologous" is indefinite. Applicants respectfully disagree, as the Examiner acknowledges the Specification provides a threshold of homology that is considered to be "substantially homologous." Office Action dated October 31, 2005; page 7. The Specification further provides exemplary methods known in the art for determining sequence homology including Swiss-PDB, sequence alignment algorithms, BLAST, and the like. Specification; page 17, lines 2 – 4. Further, the Lynch reference cited by the Examiner, claims the "SH2 domain," where "[t]he term 'SH2 domain' refers to a sequence which is substantially homologous to a Src homology region 2 ("SH2 region." (Col. 8, lines 36 – 37; emphasis added). Therefore, Applicants contend the usage of "substantially homologous" as used in the present application is definite and readily understandable to those skilled in the art in view of the present specification. In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner has also objected to the term "functional" in claim 14 and 18 as being indefinite. While Applicants further disagree with the Examiner's assertion that the term "functional" is indefinite, Applicants have deleted that term from the claims.

IV. Claims 1, 4, 6-8 and 13 Are Novel Over Lynch

Claims 1, 4, 6-8, and 13 are rejected under 35 U.S.C. § 102(b), as being anticipated by Lynch, et al., U.S. Pat. No. 6,207,397 issued March 2001, hereinafter "Lynch." Applicants have cancelled claim 8 and have amended claim 1 to require viral polymerase subunits that interact. This aspect of the claimed subject matter is neither taught nor suggested by Lynch. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection with respect to claims 1, 4, 6 and 7.

V. Claims 1, 4, 6-8 and 13 Are Not Obvious Over Keating and Zuccola

Claims 1-4, 6-11 and 13-18 are rejected under 35 U.S.C. § 103(a), as being unpatentable over Keating, et. al., *Proceedings of SPIE*, Vol. 3913, June 2000, hereinafter "Keating" in view of Zuccola, et. al., *Molecular Cell*, Vol. 5, No. 2, Feb. 2000, herein after "Zuccola." Applicants respectfully traverse the rejection in view of the amended claims now presented.

As recognized by the Examiner, Keating is directed towards fluorescence polarization assays. Specifically, Keating discloses obtaining polarization measurements with purified LFA-1 and MAC-1 with LFA-1 of the surfaces of intact cells. Keating, page 129. The Examiner notes that Keating does not teach or suggest using viral polymerase subunits or fragments thereof that interact or the screening of compounds that would inhibit such interaction.

Zuccola "describe[s] the 2.7A resolution crystal structure of the N-terminal two thirds of UL42 (UL42ΔC320), which is sufficient for all its known activities, bound to the last 36 amino acids of Pol." Zuccola, page 268; citations omitted. The Examiner believes that one of skill in the art would have been motivated to modify the fluorescence polarization method of Keating to include the viral polymerase subunits of Zuccola to arrive at Applicants' claimed method.

Applicants respectfully traverse the Examiner's rejection based on the amended claims now presented.

A *prima facie* case of obviousness requires three showings:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.

Manual of Patent Examining Procedure, 8th ed., § 2142.

Applicants respectfully submit that the present rejection lacks sufficient motivation to modify the references in the manner suggested by the Examiner because no reasonable expectation of success exists without reference to Applicants' own disclosure. The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. *In re Fritch*, 972 F.2d 1260, 1266 n.14, 23 USPQ 1780, 1783-84, n.14 (Fed Cir. 1992). One skilled in the art would not be led by either Keating or Zuccola to combine their respective teachings to produce the claimed invention with a reasonable expectation of success. The Examiner cannot use hindsight reconstruction based on Applicants' disclosure to provide motivation to combine the references. *See W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553 (Fed Cir. 1983) *cert. denied*, 469 U.S. 851 (1984).

Keating provides no reasonable expectation of success that fluorescence polarization can be successfully used to identify inhibitors of the interaction between two viral polymerase subunits or fragments thereof. Zuccola, relied on by the Examiner to modify the primary reference, likewise, provides no reasonable expectation of success.

In fact, Applicants respectfully submit that the Examiner's combination of Keating with the crystal structure determination of Zuccola represents an improper usage of the obvious-to-try situation, which is not the test for obviousness under §103. An obvious-to-try situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued. In re Eli Lilly & Co., 916 F.2d 943, 945, 14 USPQ2d 1741, 1743 (Fed. Cir. 1990). See also In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987) (where the PTO failed to establish a prima facie case of obviousness as to the appellant's claim to a method of inhibiting scale formation on and corrosion of metallic parts in cooling water systems by use of compositions containing a certain copolymer, a water soluble zinc compound and a certain acid; "[a]t best, in view of [the disclosures of the prior art], one skilled in the art might find it obvious to try various combinations of these known scale and corrosion prevention agents.")

In the instant case, the Examiner contends that Zuccola "expressly comments on the desirability of finding novel inhibitors of this interaction." Office Action dated October 31, 2005; page 11. The cited section, however, merely states in general terms that the structure described provides biochemical and genetic data that "may lead the way for the design of new antivirals." *See* Office Action date October 31, 2005; citing page 268 of Zuccola. Applicants respectfully submit that Zuccola is the type of general teaching that can only lead to an obvious-to-try situation since Zuccola is not directed to testing compounds for inhibiting herpes simplex virus DNA polymerase. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection and allowance of the claimed subject matter.

VI. Claims 1, 4-8, 12 and 13 Are Not Obvious Over Keating and Gee

Claims 1, 4-8, 12 and 13 are rejected under 35 U.S.C. § 103(a), as being unpatentable over Lynch et al. in view of Gee, et al., U.S. Pat. No. 6,162,931, issued Dec. 2000, hereinafter "Gee."

As recognized by the Examiner, Gee merely discloses the use of Oregon Green. Merely modifying the methodologies of Lynch to include Oregon Green does not teach, disclose, or suggest the subject matter of amended claims 1, 4-8, 12 and 13. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

VII. New Claims 19 and 20

New claims 19 and 20 have been added through this Response and Amendment. The new claims depend from claim 1 and further recite specific test compounds utilized in the method. Support for these test compounds can be found in the Specification. See, e.g., pages 4 - 6. Applicants submit that the subject matter of claims 19 and 20 are not taught, disclosed, or suggested, either individually or in combination, by the asserted references, and therefore respectfully request allowance of the claims.

VIII. CONCLUSION

Having addressed all outstanding issues, Applicants respectfully request entry and consideration of the foregoing amendments, and reconsideration and allowance of the case. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone the undersigned at the number below.

Respectfully submitted,

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By _____

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